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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/417,226	10/13/99	SUNDREHAGEN	E REF/SUNDREHA

EXAMINER	
HINES, J	
ART UNIT	**PAPER NUMBER**
1645	13

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DATE MAILED: 06/08/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

1- File Copy

Office Action Summary

Application No.	Applicant(s)
09/417,226	Sundrehagen et al.
Examiner	**Art Unit**
Ja-Na Hines	1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Apr 10, 2001

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1, 3-7, 9-12, 16-20, 24-33, 35, 36, 42-44, and 47-50 is/are pending in the applica

4a) Of the above, claim(s) _____ is/are withdrawn from considera

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 1, 3-7, 9-12, 16-20, 24-33, 35, 36, 42-44, and 47-50 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirem

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Continued Prosecution Application

1. The request filed on April 10, 2001 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/417,226 is acceptable and a CPA has been established. An action on the CPA follows.

Amendment Entry

2. The amendment filed January 29, 2001 was entered. Claims 1 and 4 were amended. Claims 1, 3-7, 9-12, 16-20, 24-33, 35-36, 42-44, 47-50 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 1, 3-7, 9-12, 16-20, 24-33, 35-36, 42-44, 47-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 is vague and indefinite. The preamble of claim 1 recites an assay method for the determination of transcobalamin II bound cobalamin in a body sample, however the detection step states that the cobalamin content in said cobalamin containing liquid will be determined. There is no correlation step which correlates the determining the cobalamin content to the determination of the transcobalamin II bound cobalamin.

It is unclear whether the released cobalamin concentration is being assayed or if the cobalamin bound by TC II is being assayed.

It is also unclear how to determine how much at least 3 times the amount of cobalamin is with respect to the amount of holo-TC II, if the amount of holo-TCII is unknown.

Response to Arguments

4. Applicant's arguments filed January 29, 2001 have been fully considered but they are not persuasive.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 1, 5-7, 10, 12, 16-20, 26 and 42-44, 47-48 and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over McLean et al., in view of Houts is maintained.

Applicants argues that "no one previously has been able to produce a reliable, direct quantification of holo-TC II levels in a sample", however the claims do not recite that only holo-TC II levels are being assayed. The claims broadly recite transcobalamin II which includes both TC II and holo-TC II.

Applicant also argue that the specific binding ligands recited in the claims are not limited to antibodies, however the claims do not include a limitation which prevents antibodies from being the specific binding ligands therefore, the claims embrace the use of antibodies. Therefore, McLean et al., in view of Houts teaches an assay method for determining transcobalamin bound cobalamin in a sample.

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies i.e., that the authors in no way indicate that transcobalamin II could be utilized in an assay to determine whether a subject has a cobalamin deficiency are not recited in the rejected claims. However, McLean et al., teaches that cobalamin has an established role in DNA synthesis, suggesting that cobalamin depletion is likely to result in both reduced cell proliferation and cell death and that cobalamin is useful in cancer therapy (page 241 para. 4). Also, high concentrations of cobalamin have been safely used in the clinic to overcome the effects of genetic deficiency of TC II (page 241 para. 3). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Applicants argue that the cited references do not teach the cobalamin concentration that is at least 3 times the holo-TC II concentration. However McLean et al., teaches that by adding high levels of free cobalamin, the inhibitory action of the antibodies can be reversed (page 241 para. 3). Therefore, McLean et al., teaches the use of high concentrations of cobalamin.

In response to applicant's arguments against the references individually wherein that Houts teaches specific binding ligands for binding cobalamin, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). McLean et al., teaches that the plasma protein TC II binds and delivers cobalamin (Cbl) to all cells and the TCII/Cbl complex is internalized by receptor mediated endocytosis (abstract). McLean et al., also teaches that adding high concentrations of Cbl, will promote the binding the TCII/Cbl complex. Houts teaches competitive binding methods using a solid support, detectable labels, and centrifugation steps.

Therefore, it would have been obvious at the time of applicants invention to use the monoclonal antibodies a specific binding ligands assay method using samples from human plasma or serum, where a centrifuge step is performed and cyanocobalamin in either a direct or indirect assay can be assayed with a variety of detectable signals which indicate the presence of immobilized and non-immobilized ligands.

6. Claims 9, 11, 24-25 and 35-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over McLean et al., in view of Houts and further in view of Herbert is maintained. Applicants argue that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so

found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. The arguments of McLean et al., and Houts have been discussed above.

No more then routine skill is involved in adjusting the amount of a component of a claimed process as stated in claims 3, 25 and 35-36. Neither changes in concentrations nor determining optimum concentrations which are suitable for materials have not been held to involve patentable inventions. Therefore one skilled in the art would have expected a reasonable level of success in using an assay to include the dissociation of cobalamin/ vitamin B_{12} or analogs by changing the temperature or pH as taught by Herbert with the assay method for the determination of TCII bound cobalamin sample comprising contacting a sample body fluid with an immobilized specific binding ligand like a monoclonal antibody specific for TCII or holo-TCII, separating the bound fraction from the unbound fraction and measuring the amount of holo-TCII or TCII bound cobalamin obtained as taught by McLean et al., in view of Houts because Herbert teaches that this method is known in the art.

7. Claims 4 and 49 are rejected under 35 U.S.C. 103(a) as being unpatentable over McLean et al., in view of Houts in further view of Allen et al., (US Patent 5,374,560) is maintained. Applicants arguments pertaining to McLean et al., in view of Houts have been previously discussed. Applicants argument is that there is no suggestion to combine the references. In this case, no more then routine skill would have been required to use automation as taught by Allen et al., in the assay of McLean et al., and Houts, because Allen et al., shows it to be conventional and

well known to automate assays to detect cobalamin. Furthermore, it has been held that broadly providing a mechanical or automatic assay to replace manual activity which has accomplished the same results involves only routine skill in the art (In re Venner, 120 USPQ 192).

8. Claims 27-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over McLean et al., in view of Houts in further view of Hoyle et al is maintained. See above arguments pertaining to McLean and Houts. In response to applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. In this case, it would have been obvious at the time of applicants invention to have use the antibodies of Hoyle et al., in the method of McLean et al., and Houts because the high affinity constants of the antibodies of Hoyle et al., which provide for a more sensitive assay.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines

June 6, 2001

JENNIFER E. GRASER
PRIMARY EXAMINER